

Abuse Potential of Hydrocodone in Human Studies

Sharon L. Walsh, Ph.D.
Center on Drug and Alcohol Research
University of Kentucky

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Outline

- Abuse potential vs. abuse liability
- Human laboratory approach
 - Populations and methods
- Results from published studies
 - Normal volunteers
 - Opioid abusers
- Summary of results

Abuse Potential vs. Abuse Liability

■ Abuse Potential

- Characterizes the ability of a CNS-active drug to produce positive psychoactive effects
 - may include sedation, euphoria, perceptual and other cognitive distortions, hallucinations and mood changes.
- These effects are viewed as correlated with or predictive of the risk of abuse and/or addiction

Abuse Potential vs. Abuse Liability

■ Abuse Liability

- Is similar and sometimes used interchangeably
- Includes abuse potential
- Captures other factors, including ease of synthesis and drug abuse/diversion history
- Describes abuse potential in a social and public health context

How Are They Measured?

Abuse Potential:

Measured in the Laboratory

Non-humans

self-administration

physical dependence testing

Humans

direct drug administration

Abuse Liability:

Measured also in Community

Surveillance data from various reporting sources, including hospitals, treatment centers, national surveys, medical examiner deaths

Human Abuse Potential Studies: General Methods

- Enroll adult volunteers with appropriate drug use histories (preferably as inpatients)
 - opioid abuse histories (but without physical dependence)
- Include tests of the appropriate control (positive and negative if available) agents for comparison with the test drug of interest
 - Control condition(s) full mu opioid agonist
- Double-blind testing is employed

Human Abuse Potential Studies: General Methods

Collect a comprehensive array of outcomes

- Physiological
 - Respiratory, cardiovascular, pupil diameter
- Subjective measures
 - Visual analog questionnaires
 - Adjective scales
 - Street value estimates
- Observer-rated effects
- Cognitive/psychomotor tasks
 - Assess impairment

Contemporary Studies of Hydrocodone Available for Review

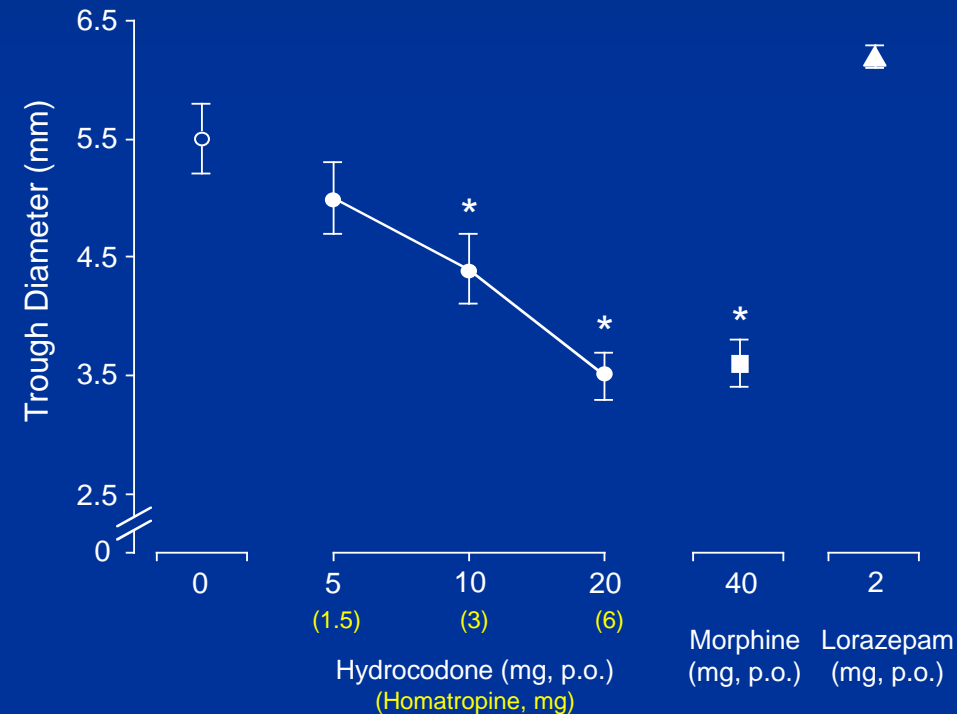
- Six human abuse potential studies of hydrocodone [published between 2003 to 2010]
- Five of oral hydrocodone
 - Hydrocodone/homatropine (Hycodan®) (n=1)*
 - Hydrocodone/acetaminophen (n=3)*
 - Hydrocodone alone (n=1)
- One of intravenous hydrocodone alone
- All studies employed within-subject, crossover designs

*Conducted in healthy non-drug-abusing volunteers

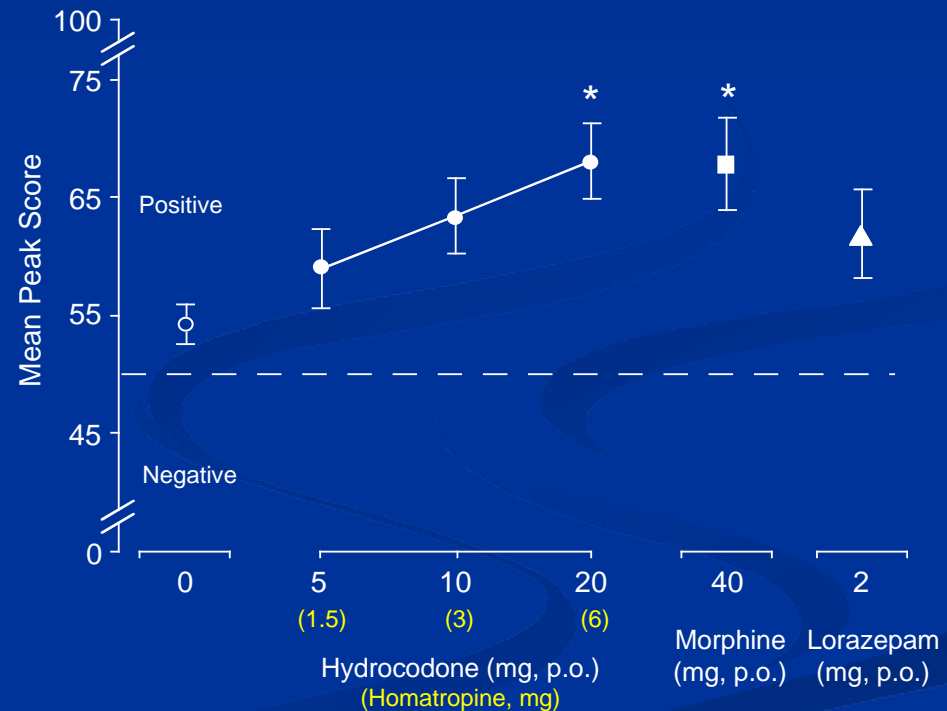
Hydrocodone/Homatropine: Hycodan®

Healthy Volunteers

Pupil Diameter

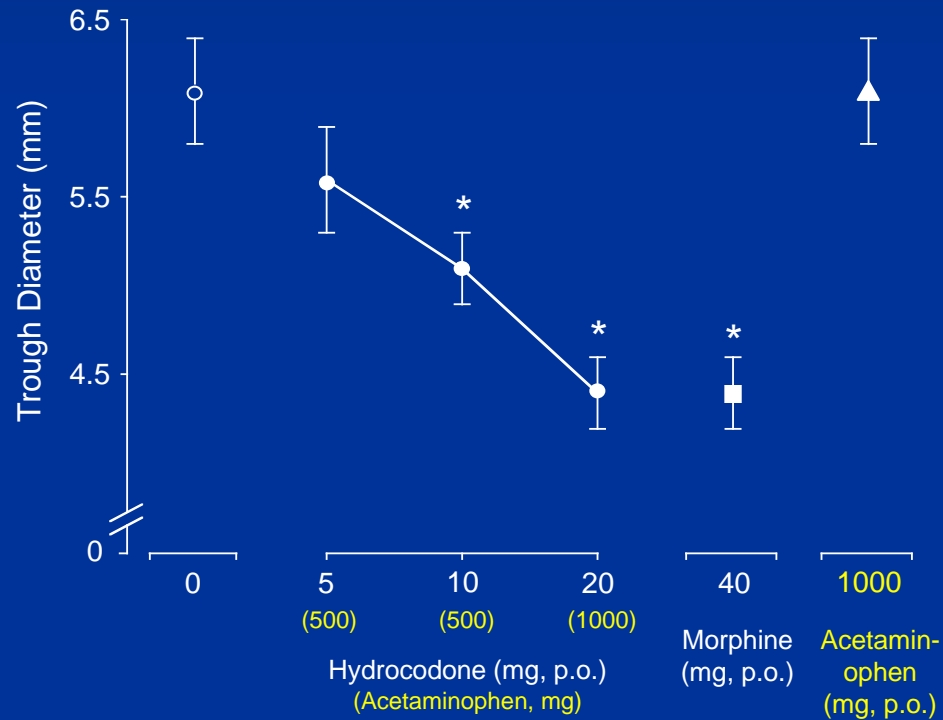


“How Much Do You LIKE the Drug?”

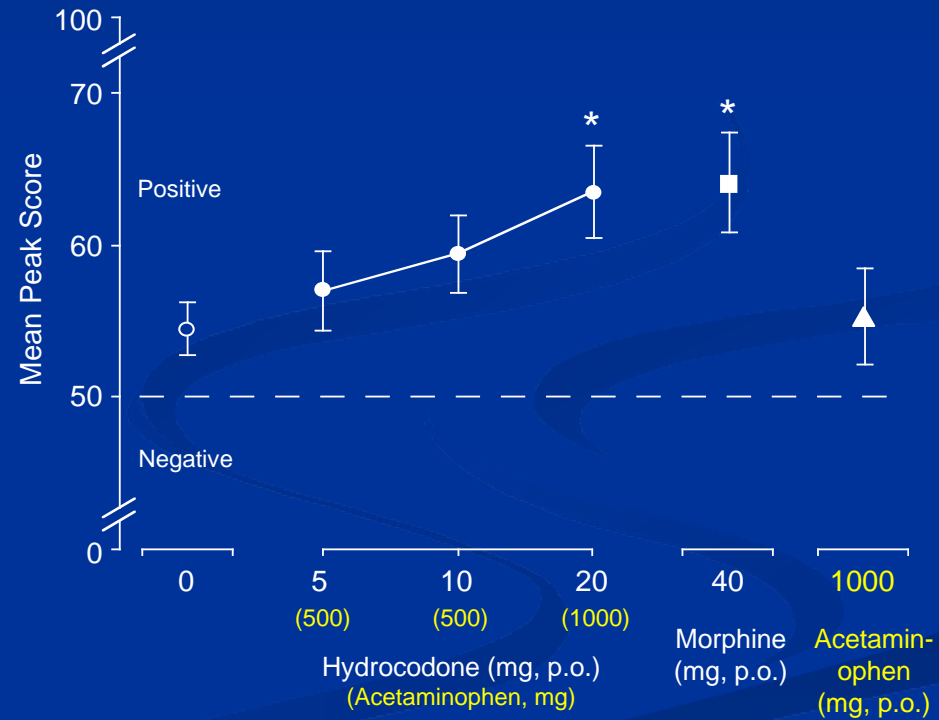


Hydrocodone/Acetaminophen Healthy Volunteers

Pupil Diameter

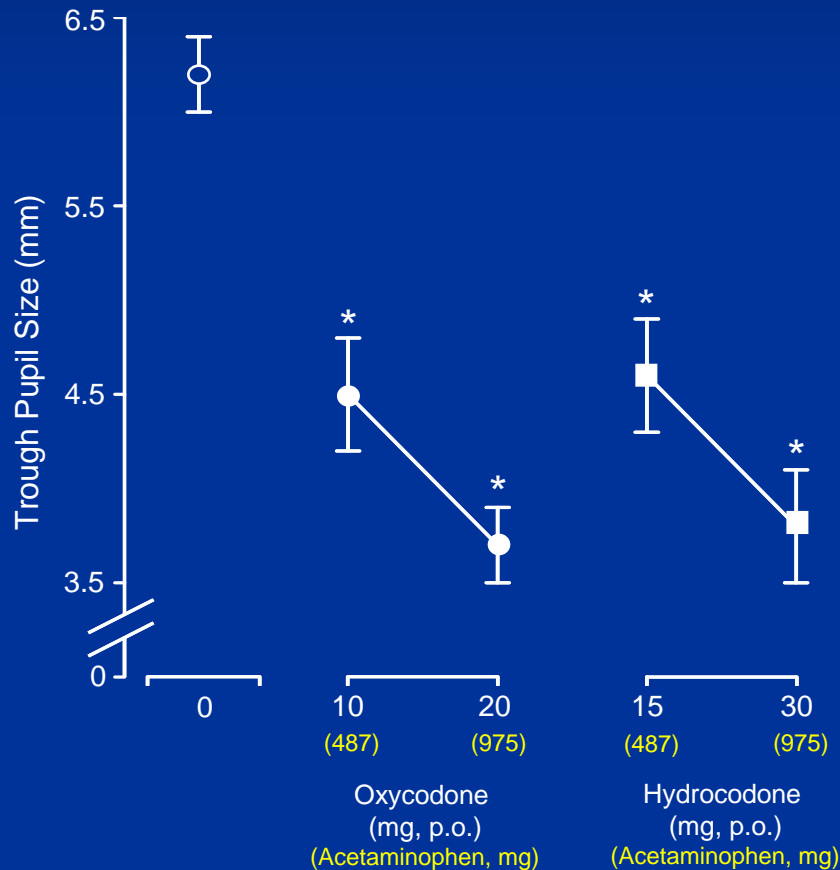


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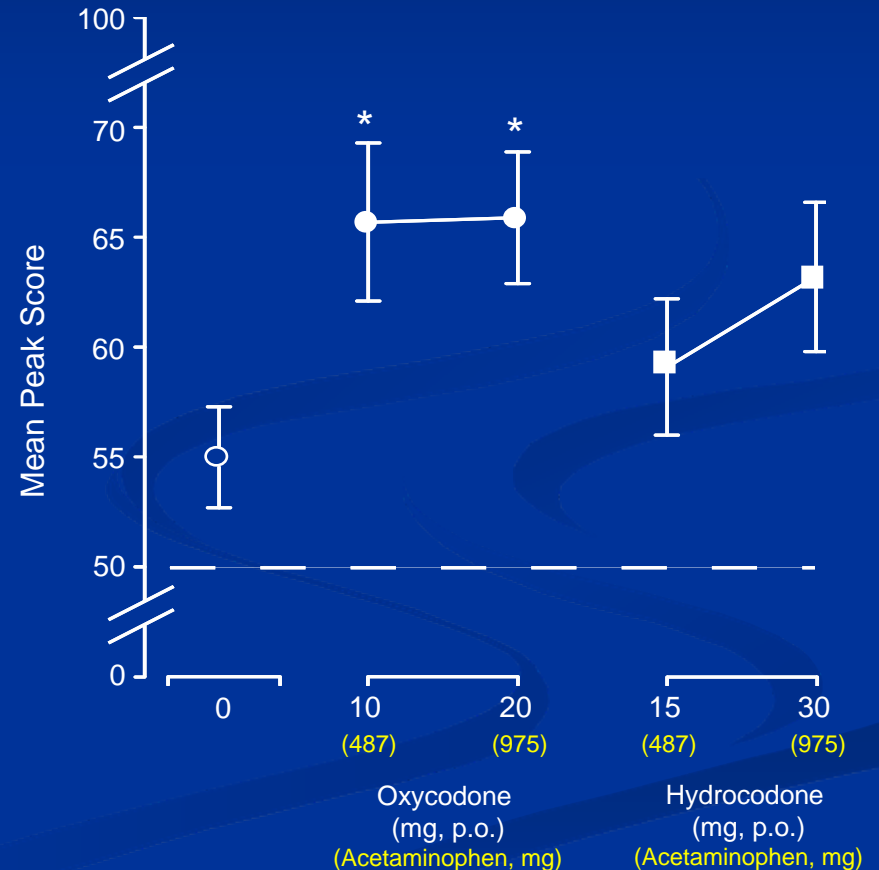


Hydrocodone/ACET & Oxycodone/ACET Healthy Volunteers

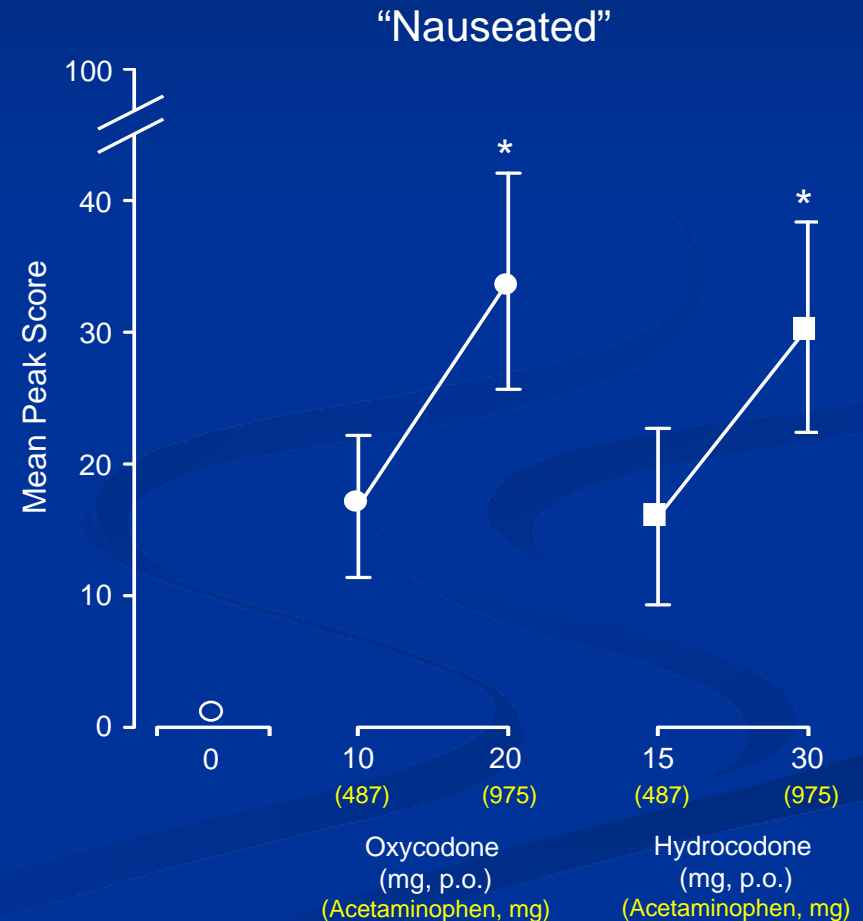
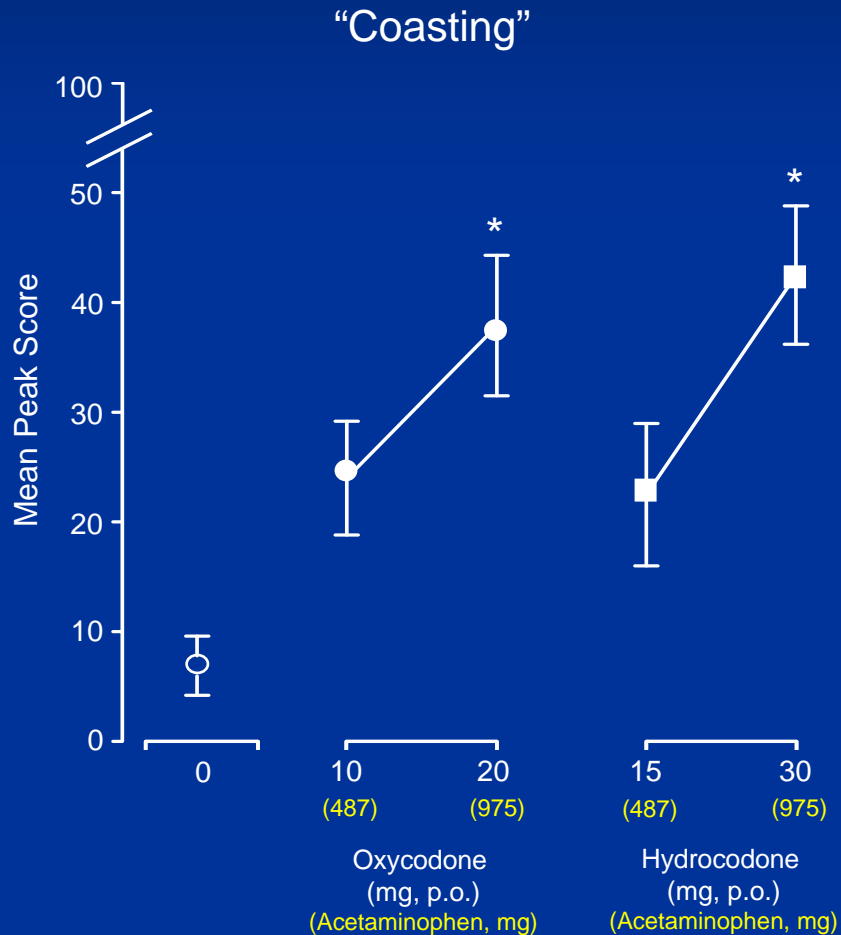
Pupil Diameter



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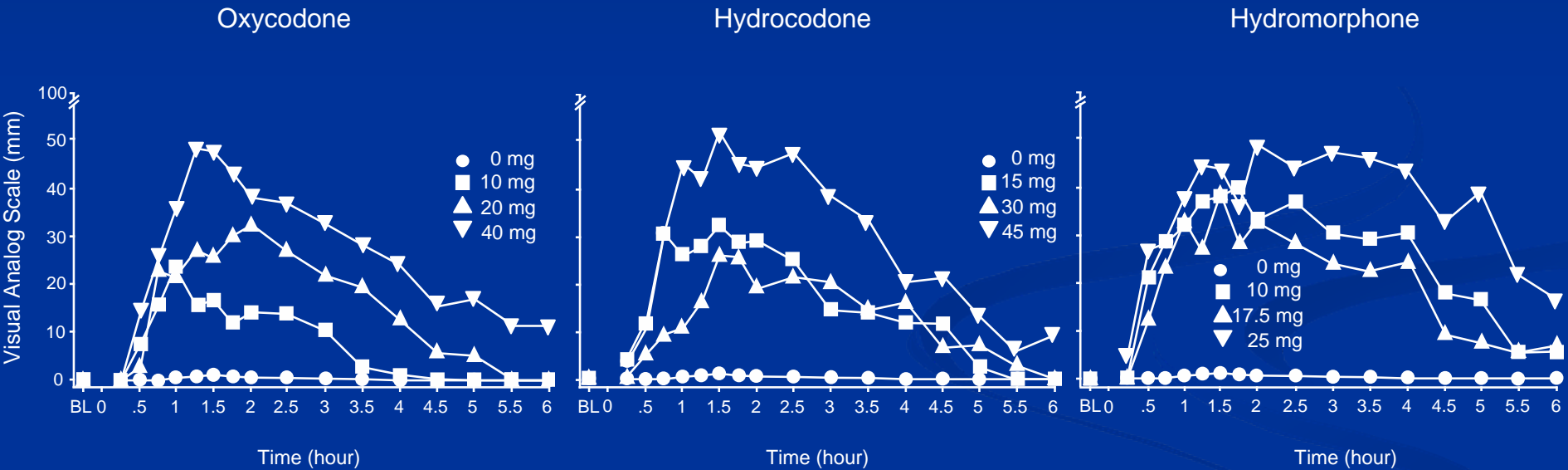


Hydrocodone/ACET & Oxycodone/ACET Healthy Volunteers



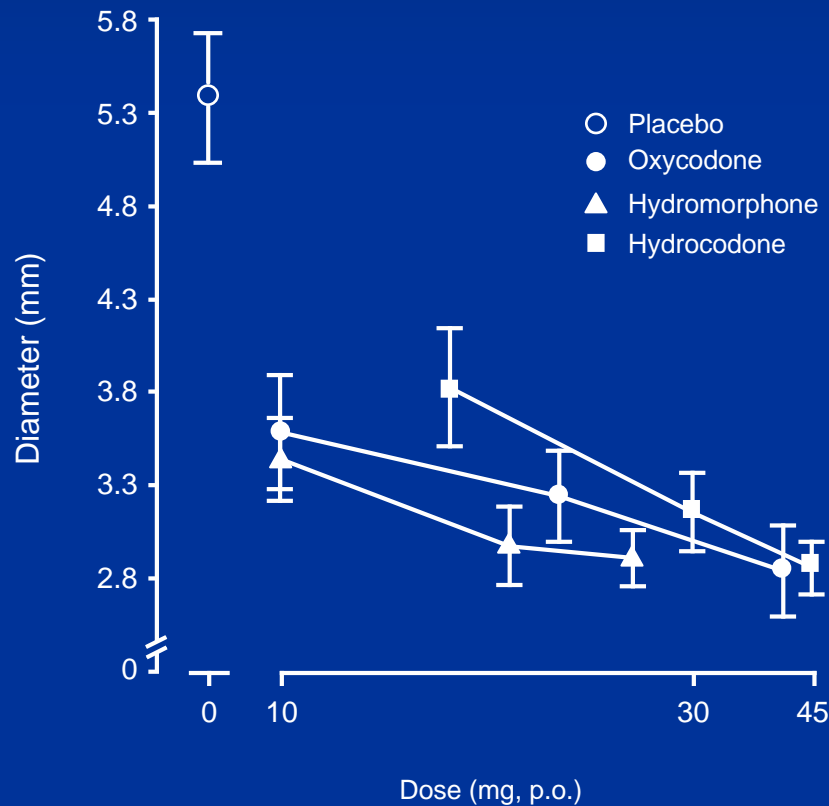
Oxycodone, Hydrocodone & Hydromorphone Prescription Opioid Abusers

“How Much Do You LIKE the Drug?”

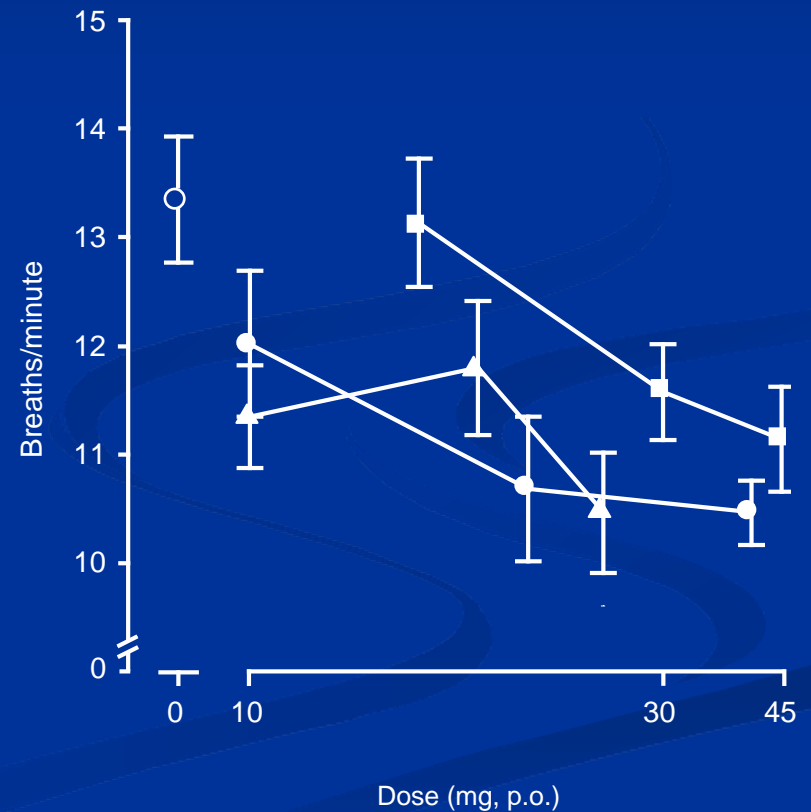


Oxycodone, Hydrocodone & Hydromorphone Prescription Opioid Abusers

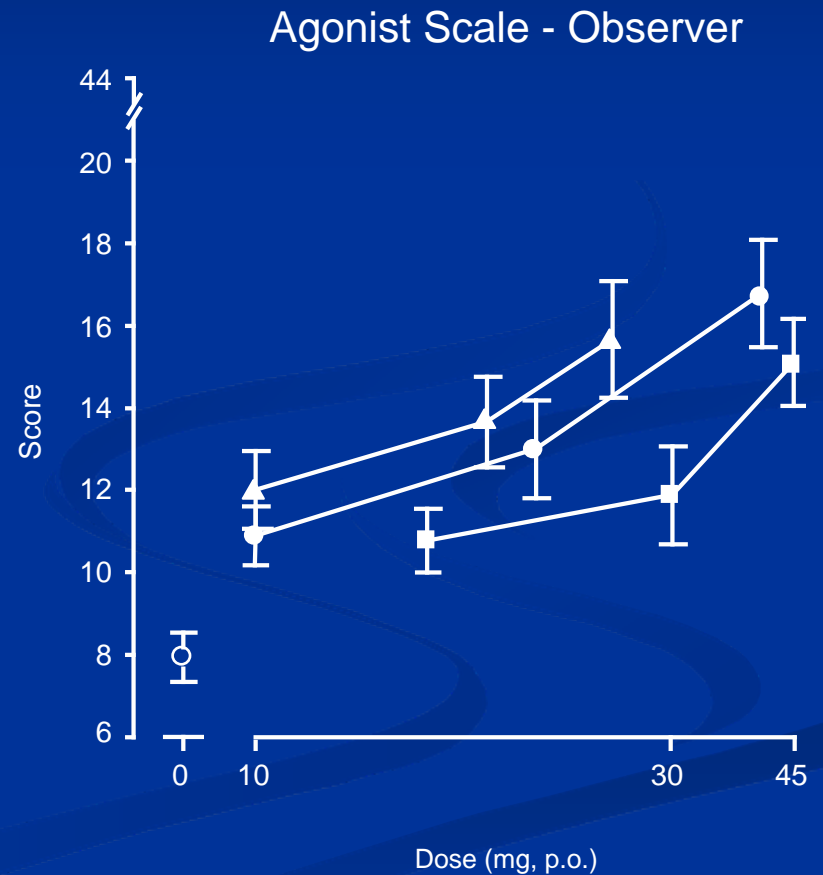
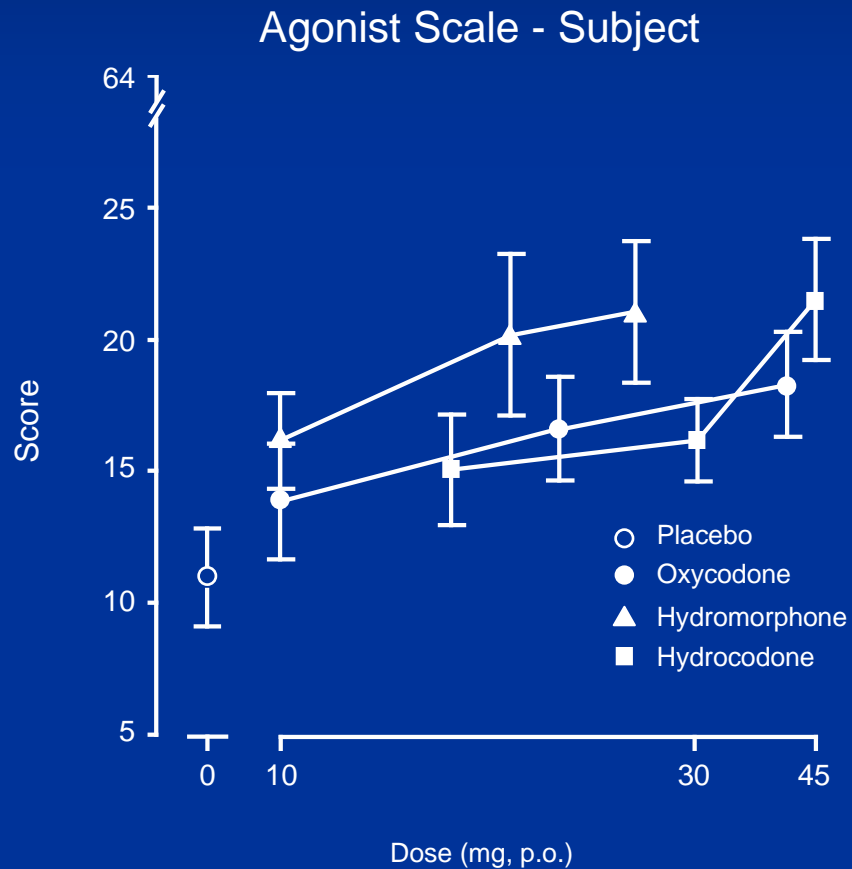
Pupil Diameter



Respiratory Rate



Oxycodone, Hydrocodone & Hydromorphone Prescription Opioid Abusers



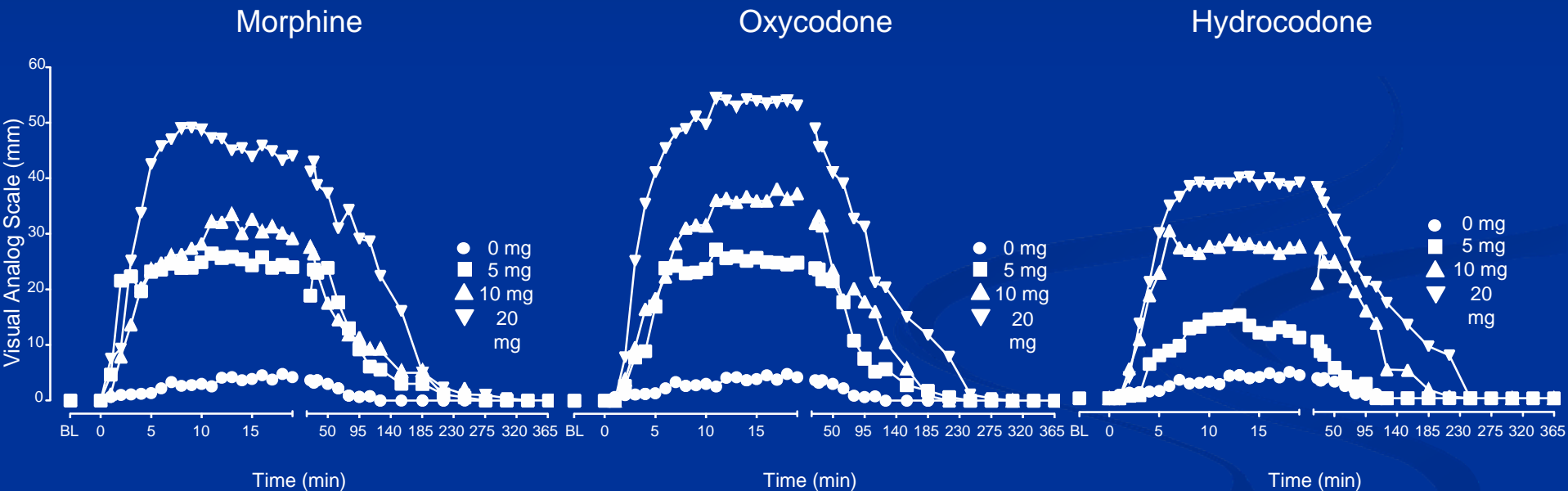
Relative Potency Estimates

- Only variables meeting the criteria for a valid bioassay were included (Finney, 1964)*
- Mean relative potency estimates across outcomes

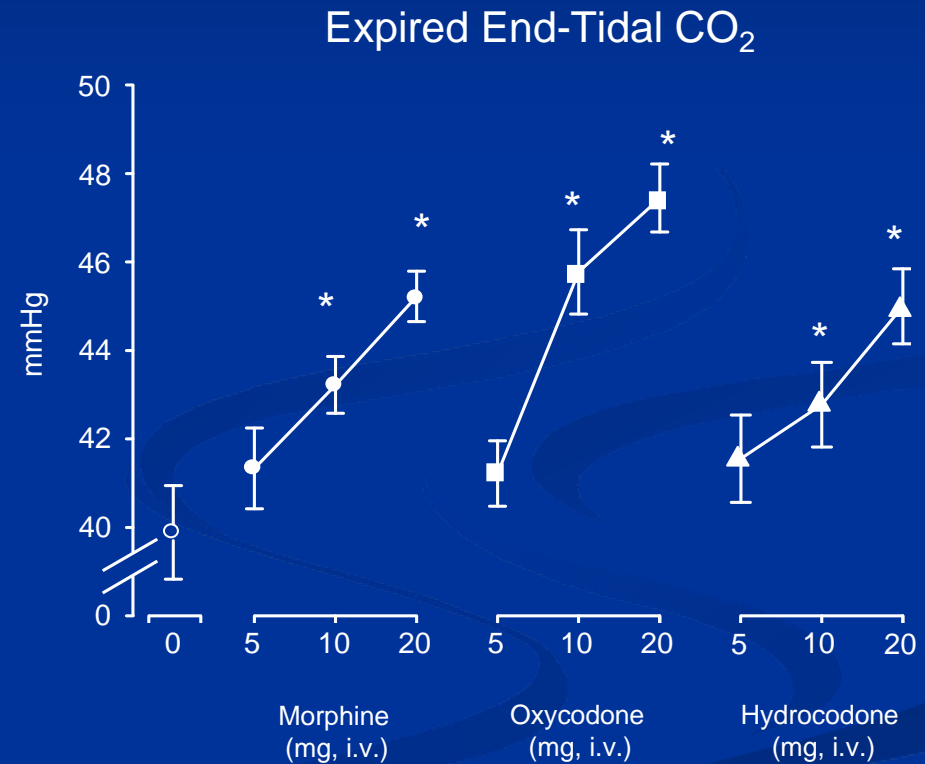
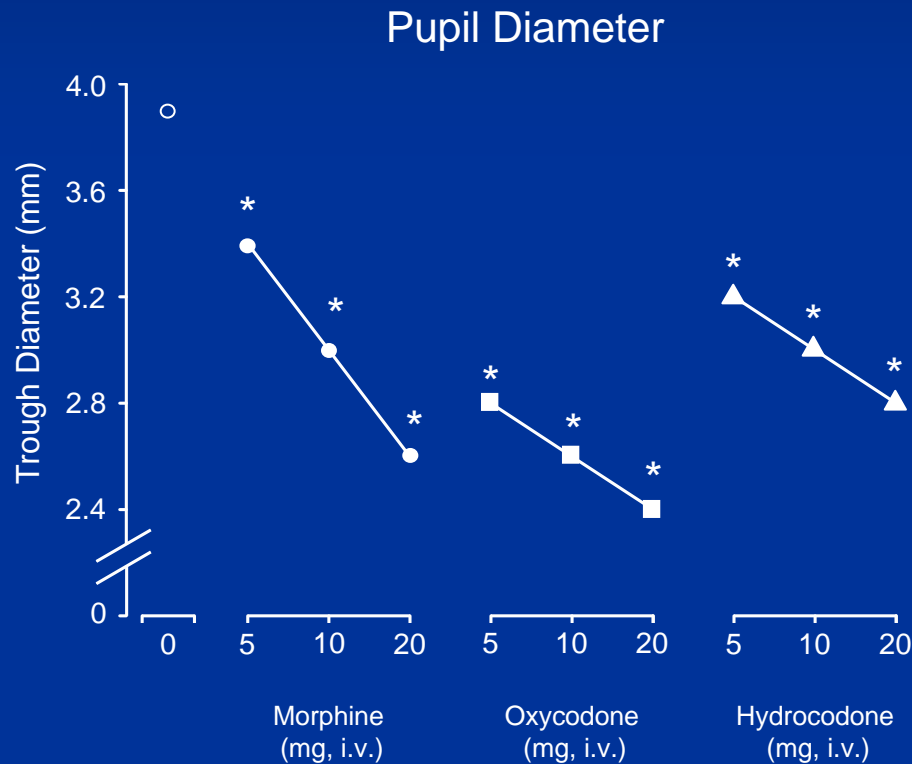
Oxycodone : Hydrocodone = 0.93 mg : 1 mg

Intravenous Morphine, Oxycodone & Hydrocodone Prescription Opioid Abusers

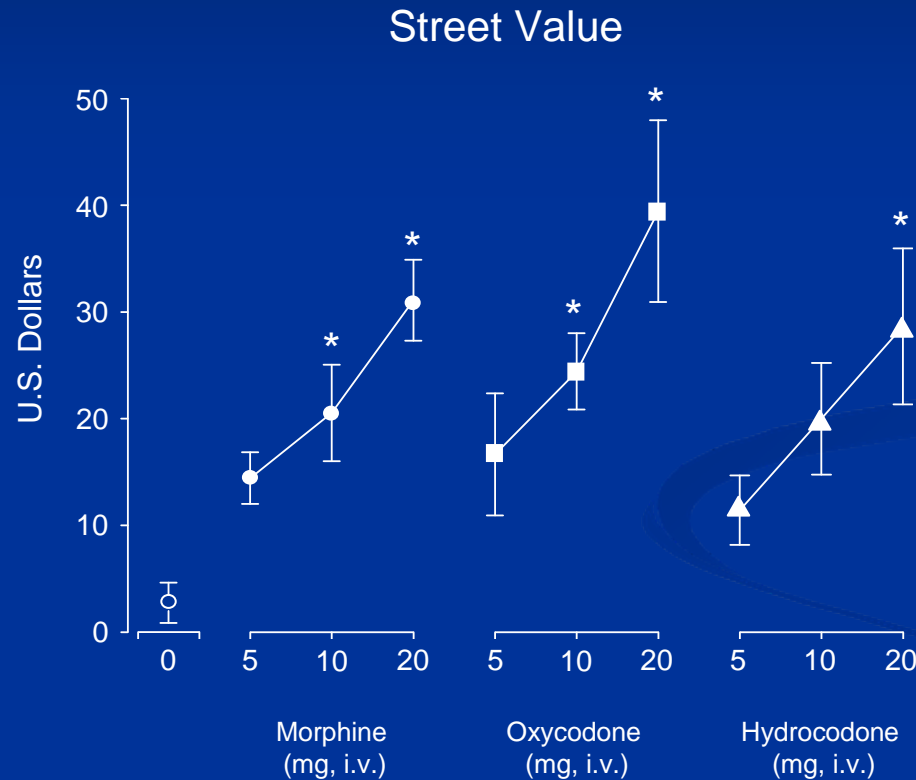
How Much Do You LIKE the Drug?



Intravenous Morphine, Oxycodone & Hydrocodone Prescription Opioid Abusers



Intravenous Morphine, Oxycodone & Hydrocodone Prescription Opioid Abusers



Summary: Studies in Healthy Volunteers

- Hydrocodone (in combination with homatropine or acetaminophen) produces dose dependent euphorigenic effects
- These effects are similar to those of morphine and oxycodone
 - Hydrocodone 20 mg ~ Morphine 40 mg
 - Hydrocodone 30 mg ~ Oxycodone 20 mg
- ACET produces no discernible effects alone
- Unpleasant effects (e.g., nausea, dizziness) occurred at the upper end of the hydrocodone dose range (as with other opioids)

Summary: Studies in Prescription Opioid Abusers

- Hydrocodone produces dose dependent increases on ratings of positive subjective reports, including ratings of liking, good effects and endorsements of street value
- There is little to no evidence that hydrocodone produces reports of negative or unpleasant symptoms
- Hydrocodone is only slightly less potent than oxycodone on subjective effects related to abuse potential
- The profile of hydrocodone is similar to comparator opioids, including morphine, hydromorphone and oxycodone